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HOW DO BACTERIA CAUSE PYREXIA? (FROM DROPLETS TO ZOONOTIC

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ABSTRACT

"Fever is most common systemic manifestation of the inflammatory response and cardinal symptoms of infectious diseases and are subject to physical and chemical stimuli"

Possible mechanism of fever production is the ultimate regulators of body temperature are the thermoregulatory centers in the hypothalamus. The causative agent in scarlet fever is Gropup A Streptococcus (GAS) AS, a gram-positive coccus that grows in chains.

The bacteria is the causative agent of strep throat, impetigo, erysipelas, cellulitis, and necrotizing fasciitis. Brucella melitensis is the most aggressive strain which produces malignant type of human disease. The fever usually rises in the afternoon. Its fall during the night is accompanied by drenching sweat. Bartonella bacilliformis causes Oroya fever. It is transmitted through sand flies. The Pontiac fever illness shows high fever, chills, malaise, nonproductive cough, hypoxia, diarrhea, and delirium. Typhoid fever syndrome is produced mainly by S. typhi,S. paratyphi. Stepladder like fever. The development of ARF (Acute rheumatic fever) occurs approximately two weeks after S. pyogenes infection Acute rheumatic fever is a delayed sequela of pharyngitis due to Streptococcus pyogenes, which are also called group A Streptococcus or group A strep.Q fever is a disease caused by the bacteria Coxiella burnetii. This bacteria naturally infects some animals, such as goats, sheep, and cattle.

KEYWORDS: Bartonella henselae, Streptococcus pyogenes, Pontiac fever, Rickettsia prowazekii, Salmonella typhi and para typhi A,B and C, Borrelia burgdorferi,Coxiella burnetii.

INTRODUCTION:

Scarlet fever is a disease caused by *Streptococcus pyogenes* (1)

Rheumatic fever may occur following an infection of the throat by the bacterium Streptococcus pyogenes (2)

Brucellosis is a highly contagious zoonosis caused by ingestion of unpasteurized milk or undercooked meat.(3)

The clinical spectrum of *Bartonella henselae* infection varies, ranging from classic cat scratch disease with only lymphadenopathy. (4)

Pontiac fever is caused by Gram-negative bacteria in the genus Legionella. (5)

Tuberculosis (TB) is one of the oldest diseases and today, it is one of the most common infectious diseases, especially in developing countries. Tuberculosis is the second cause of death after HIV in infectious diseases and in 1993, WHO, declared TB as a "global health emergency " (6).

According to the WHO reports presented in 2014, 9 million new cases of Tuberculosis (pulmonary and extrapulmonary types) were detected worldwide (7)

Q fever or query fever is a disease caused by infection with *Coxiella burnetii*. (8)

Q fevers are extremely rare and most often manifest as culture-negative endocarditis in patients with underlying valvular heart disease (9)

Rickettsia prowazekii and Bartonella quintana, Borrelia recurrentis, the body louse, is a vector. (10)

The two most common disease manifestations of human Salmonella infections are gastroenteritis and typhoid fever. *S. Typhi and S. Paratyphi A,* can cause typhoid fever, a more severe systemic disease (11)

Enteric fever is caused by *Salmonella typhi and para typhi A,B and C* is a significant cause of morbidity and mortality (12)

The typhoid fever surveillance in Africa program (TSAP) revealed a significant burden of Salmonella disease in sub-African Sahara Africa (13)

Salmonella enterica, is responsible for systemic enteric fever illnesses in >20 million people worldwide each year. (14)

Symptoms of typhoid include fever, headache, weight loss, lethargy, stupor, malaise, leukopenia, thrombocytopenia, gastrointestinal bleeding, and neurological complications (15)

Chronological record of significant events:

For many centuries, Streptococcal diseases have been known. The 4th century BC erysipelas was described in the original writings of Hippocrates. It was not until the 18th century that further progress into the etiology of diseases was made. A major advancement was the invention of the microscope by Anton van Leeuwenhoek (1632-1723) as well as his descriptions of new life forms, including the shapes of cocci, bacilli, and - Ferretti J, Köhler W. History of Streptococcal Research. 2016 Feb 10. In: Ferretti JJ, Stevens DL, Fischetti VA, editors. Streptococcus pyogenes : Basic Biology to Clinical Manifestations [Internet]. Oklahoma City (OK): University of Oklahoma Health Sciences Center; Add history of Strep as well, if you wish. 2016-

Hippocrates, writing around 400 BC, described the condition of a person with a reddened skin and fever (16)

Eberth,1880 first observed the typhoid bacillus in mesenteric lymph nodes and spleen in fatal cases of typhoid fever.

Pasteur isolated Staphylococcus aureus in 1880. However, scientists discovered that the use of penicillin could cure S. aureus.(17)

Bartonella bacilliformis causes Oroya fever. It was named after an epidemic of the disease in 1870,during railway construction between Lima and Oraya in South America.

Pontiac fever was named for Pontiac, Michigan, where the first case was recognized(18) Hensen,in 1868 discovered the first member Lepra bacillus.

Robert Koch isolated mammalian tubercle bacillus and Johne, 1895 describe My paratuberculosis Salmonellae are gram-negative motile bacilli. The genus Salmonella, which belongs to the family Enterobacteriaceae. Daniel E. Salmon,first isolated Salmonella from in 1884.(19)

Salmonella was named after Daniel Elmer Salmon (1850–1914), In 1884, pathologist Georg Theodor August Gaffky (1850–1918) confirmed Eberth's findings. (20)

British bacteriologist Almroth Edward Wright first developed an effective typhoid vaccine at Nutley, Hampshire. (21)

Wright convinced the British Army, that 10 million vaccine doses should be produced for the troops being sent to the Western Front, thereby saving up to half a million lives during World War (22)

For the first time, their casualties due to combat exceeded those from disease (23) *Borrelia burgdorferi,* was identified in 1975 in Lyme, USA. Borrelia is a genus of bacteria of the spirochete phylum. It causes Lyme disease, also called Lyme borreliosis, a zoonotic, vector-borne disease transmitted primarily by ticks and by lice.(24)

Coxiella burnetii, is smaller than Rickettsiae, passes through porcelain filters and causes Q-fever or "Query" fever, Q fever was first described in 1935 by Edward Holbrook Derrick in slaughterhouse workers in Brisbane, Queensland.(25)

David Bruce,a military doctor first isolated Brucella organism,the causative agent of Mediterranean fever,undulant fever and Malta fever Maltese scientist and archaeologist Themistocles Zammit identified unpasteurized goat milk as the major etiologic factor of undulant fever in June 1905.(26)

Robert Koch identified and described the bacillus causing tuberculosis, M. tuberculosis, on 24 March 1882 (27)

Research on the role of interleukins in bacterial pyrexia:
Interleukins or Lymphokines are regulatory proteins secreted by monocytes or macrophages or T-lymphocytes.They are involved in signalling between cells of the immune system.Interleukins are a group of biologically active factors released by primed lymphocytes.Lymphokines can be secreted by both T and B lymphocytes,though T cells are assumed to be the main source.These are non-antibody proteins and polypeptides secreted by lymphocytes on contact with antigen.They act as intercell mediators in immune responses.There are many lymphokines which have a wide range biological activities. Many lymphokines show multiple biological activities and so the descriptive names can be misleading.

A nomenclature interleukin is introduced followed by a number.Interleukin-1(IL-1). This was originally called as lymphocyte activating factor (LAF) Initially, it was observed to be secreted by monocytes and macrophages (hence known as monokine), but now it is known to be produced by all nucleated cells .The production of interleukin-1 is introduced by the antigens,lectins and lymphokines from T- cells such as macrophage activating factor.IL-1 stimulates B-cell proliferation,differentiation and synthesis of immunoglobulins.It activates T-cells and promote synthesis of lymphokines.It is endogenous pyrogen, hence induces and stimulates an increase in acute phase serum proteins.(28) IL-1 consists of two proteins.IL-1 alpha,and IL-beta,both have exactly the same functions.IL-1 is produced byall antigen presenting cells,but activated macrophages and monocytes produce the same in relatively large amounts.IL-1 thus liberated from activated macrophages, binds to its high affinity receptors on the enlarged T-cells leading to rapid internalization of IL-1.The IL-1 readily inducesRNA and protein synthesis of the responsive T-cells. The cell enlarges to a blast like appearance.

Mechanisms of fever induced by recombinant human interferon:
Certain symptoms of infections, such as fever, muscle pain and "flu- like symptoms", are also caused by the production of IFNs and other cytokines. (29)

Interleukin -1 receptors are present on diverse cells and activate CD-4 T cells Activation of resting CD-4 T-cells requires two signals; First is the antigen in association with class 11 molecules and second is the internalization of IL-1.IL-1 binds to its high affinity receptor on T- cells by antigen MHC,leading to rapid internalization of the IL-1The internalizedIL-1 now readily induce RNA and protein synthesis of the responsive cell.The cell enlarges to a blast like appearance Removal of bacteria from blood The body possesses remarkably efficient mechanisms for sterilizing the blood stream.Most bacteria are less capable of causing disease when injected intravenously than given by any other route.With most bacterial species,a large number of living organisms can be swiftly cleared from the circulation.

In general, although a few bacteria may persist for some time, all disappear completely within an hour or so. The main exceptions are provided by the encapsulated virulent strains of Streptococcus pneumonia, Klebsiella pneumoniae and Bacillus anthracis. With an average 24 hour culture of virulent type of the pneumococcus, organisms will have lost their capsules and consequently the initial drop of organisms may assume the usual rapid fall, leaves a few encapsulated forms which persists, and their multiplication produces a climb which may eventually result in death in septicemia. Most of the bacteria removed from blood after single injection are found in the macrophages of the liver and spleen. By collecting arterial samples from femoral artery and venous samples from several sites by an intravenous catheter, it has been found that the bacterial count of the arterial blood remains stable, and was no evidence of removal of bacteria from the blood circulating through the extremities, or the kidney, but as blood passed through the liver a dramatic reduction in bacterial count occurred.

Role of polymorph nuclear leucocytes in clearing the bloodstream:
Although most of the bacteria removed from the circulation find their way to the liver and spleen. Some organisms can be seen to enter the polymorph nuclear leucocytes, and clump the cells laden with bacteria can be seen within the capillaries of various organs, especially the lungs, the probable destination of such cells is to the macrophages of the reticuloendothelial system, which finally dispose of both macrophages and bacteria. However, in certain stages of the clearance process the lung may also play a role in the removal of circulating bacteria. The intravenous injection of Staphylococci produce a profound leukopenia. Almost all the circulating macrophages disappear from the blood for about 20 mnts, most lodge in the lung capillaries where they may still be capable of clearing bacteria from the blood Rabbits which are rendered leucopenia by whole body X-ray treatment maintain high levels of organisms in blood following intravenous injection of E. coli far longer than do normal animals, however such leucopenic animals are transfused with healthy rabbit leucocytes, subsequent injections of E.coli are cleared normally. This occurs despite the fact that the transfused leucocytes have disappeared from blood.

These facts suggest that polymorphonuclear leucocytes accumulating within the pulmonary capillary bed may create a progressively efficient supplementary fiter. (30) The relation if inflammatory response to defence Fever is most common systemic manifestation of the inflammatory response and cardinal symptoms of infectious diseases. Possible mechanism of fever production is the ultimate regulators of body temperature are the thermoregulatory centers in the hypothalamus. They are subject to physical and chemical stimuli. Direct mechanism of injury or the application of chemical substances to these centers results in fever. Neither of these obvious forms of stimulation is present in the many types of fever that are associated with infection, neoplasms, hypersensitivity, and other processes that cause inflammation. Among substances capable of inducing fever are the endotoxins of gram negative bacteria and extracts of cells-especially monocytes and macrophages- called Interleukin-1.

The temperature dependence of many microorganisms is well known and tubercle bacilli, pathogenic for mammalian species, will not infect cold blooded animals. Conversely, the mycobacterium parasite on cold blooded animals, eg. Myco.marinum,cannot cause deep or systemic infections in man. Fowls which are naturally immune to anthrax can be infected if their temperature is lowered, Gonococci and Treponemes are readily killed at temperatures over 40 degrees C and fever therapy was used in chronic gonococcal infection and cerebral syphilis before introduction of antibiotics The neisseriae and treponemes are also susceptible to temperatures around freezing point.The smallpox virus, which has a ceiling temperatures of 38.5degrees C, grows mainly in cooler skin, causing a rash, during the febrile phase of the infection, though it grows internally, probably in the respiratory tract during the afebrile incubation period. It is therefore apparent that temperature is an important factor in determining the innate immunity of an animal to some infective agents and it seems likely that the pyrexia which follows so many different types of infection can function as a protective response against the infecting microorganisms.

The Mechanism Involved in Typhoid Fever/Enteric Fever/Mycobacterium Fever:
Endemic fever is endemic in many developing countries due to poor sanitation and substandard water supply. Enteric fever is caused due to infection by the genus Salmonella which comprises of Salmonella typhi, Salmonella Para typhi A, Salmonella Para typhi B, Salmonella Para typhi C, all these organisms can cause a bacteremic illness known as enteric fever.

In the initial stages of infection, the pathogen invades small and larger bowl walls, creating an inflammatory response. It is an intracellular pathogen. The infection spread through the body via the regional lymph nodes and bloodstream. Initial symptoms of infection are headache, fever, general malaise of infection and abdominal tenderness. Once the organism has spread throughout the body, it reaches the gallbladder and peyer's patches in the colon, initiating the diarrheal stress of illness. The organism can frequently be recovered from blood and stool cultures. Appropriate antibiotic use results in clinical improvement, however, stool cultures often remain positive, which can serve as a source of infection for other individuals.

Some patients can develop chronic colonization of their gallbladder, biliary tree leading to persistent shedding of the organism with potential transmission to others (31)

In addition, M. tuberculosis uptake can cause apoptosis of macrophages, and this could play a role in adjacent tissue damage (32)

Differential diagnosis of pyrexia:
Most febrile illnesses are due to infection and often the diagnosis can be made by clinical examination alone. In other instances a diagnosis may require confirmation by haematological examination, radiography, scanning, bacteriological or serological investigation of blood or other body fluids, discharges or excreta. Often, detection of specific antibodies in the serum may have to be undertaken before the diagnostic problems may be solved. Occasionally the cause of a febrile illness remains uncertain in spite of investigation and such a case is categorised PUO (Pyrexia of unknown origin). To establish the diagram, enquire again, the patient has lived or travelled overseas. Repeat the examination of the patient for new signs if any. Examine urine repeatedly for protein, white and red blood cells and microorganisms. Inspect the temperature charts for evidence of some characteristic appearance such as the undulations seen in some cases of lymphoma or the periodicity of malaria. Review the results of laboratory investigations, thoroughly recrutinise any radiographs and repeat such examinations as may seem necessary (33)

Hypothalamus:
Temperature is regulated in the hypothalamus. The trigger of a fever, called a pyrogen, results in the release of prostaglandin E2 (PGE2) (34)

Norepinephrine increases thermogenesis in brown adipose tissue, and muscle contraction through shivering raises the metabolic rate (35)

Biotechnology of Molecular Diagnosis of Fevers:
Detection methods rely on traditional bacterial culture procedures on selective-differential agar plates (36)

DNA fingerprinting techniques, such as pulsed-field gel electrophoresis (PFGE), ribotyping and intergenic sequence (IGS) ribotyping have all been used to subtype Salmonella isolates. (37)

The regions are amplified by polymerase chain reaction (PCR) before gel electrophoresis is done. (38)

The DNA fragments are separated on an agarose gel subjected to a pulsed electric field. (39).

Studies have reported excellent sensitivity and specificity when compared to positive and healthy controls. The turnaround time for diagnosis has been less than 24 hours. (40)

Laboratory diagnosis of Bartonella, is established by culture, serology, or histopathology. Molecular techniques such as PCR are useful for blood and tissue specimens.

Molecular techniques such as PCR are useful for blood and tissue specimens, including heart valves, where available

Researchers struggle to develop a new treatment for Enteric fever/Typhoid fever:
Patients with persistent vomiting, inability to take oral food, severe diarrhea, and abdominal distention usually require parenteral antibiotic therapy preferably in a hospital. Antibiotic therapy must be guided by invitro sensitivity testing.

Chloramphenicol (500 mg 4 times daily), Ampicillin (750 mg 4 times daily) and co-cotrimoxazole (2 tablets or 1V equivalent twice daily) are losing their effectiveness due to resistance in many areas of the world, especially India and South East Asia. Fluoroquinolones are the drug of choice (Eg Ciprofloxacin 500 mg twice daily) if nalidixic acid screening predicts susceptibility, but resistance is common, especially in the Indian subcontinent and also in the UK.

Extended-spectrum of cephalosporins are useful alternatives but have slightly increased treatment failure rate. Azithromycin 500 mg once daily is an alternative when fluoroquinolone resistance is present. Salmonella resistant to chloramphenicol can respond to norfloxacin, ciprofloxacin therapy. For gastroenteritis in uncompromised hosts, antibiotic therapy is often not needed and may prolong the convalescent carrier state. for enteric fever appropriate antibiotics in which beta-lactams and fluoroquinolones.

With the limitations of the two existing *Salmonella* vaccines, particularly their lack of effectiveness in young children, along with their lack of widespread uptake in endemic countries, the *Salmonella* community and global health policymakers are keenly awaiting the arrival of new vaccines against *Salmonella* Vaccine is indicated for those persons who travel or live in ares where typhoid fever is endemic. Three types of vaccines are available 1. Killed whole –cell vaccine 2.

Live oral (Ty2 1a) typhoid vaccine 3. Purified V1 poly saccharide vaccine (V1CPS) Multi drug resistance transmitted genetically by plasmids among the srains of S.typhi has been reported for the first time in 1972 from Mexico. The transmissible plasmids carry R determinants to chloramphenicol, streptomycin, and sulphonamide and tetracycline. Multiple drug resistance has become a problem in India and South East Asia. Chloramphenicol resistant typhoid fever had appeared first in epidemic form in Kerala (Calicut) India in 1972. The drug resistant strains os S.typhi that had been reported from India were originally confined to include phase D1-N,but later to types C5, A and O (41)

Table 1: Current treatments to common bacterial fevers

Bacterial fever	Current treatment (Drug of choice varies according to specific in vitro sensitivities) (1)
1. Scarlet fever and or Rheumatic fever Group A *Streptococcus pyogenes*	Penicillin G Penicillin VK Amoxicillin Cephalosporins • Cephalexin • Cefdinir • Cefpodoxime Macrolides in Penicillin allergic patients (5) • Erythromycin • Azithromycin Clindamycin (potent inhibition of toxin production) Vancomycin
2. *Staphylococcus aureus* induced fever	Cephalexin Clindamycin Doxycycline or minocycline TMP-SMZ Cefazolin (MSSA)

	Vancomycin (vs MRSA) (3) Daptomycin Macrolides only in documented in vitro sensitivity Linezolid (vs MRSA) (3) Tedizolid Tigecycline Ceftaroline (vs MRSA) Dalbavancin Oritavancin Telavancin Nafcillin (MSSA) Oxacillin (MSSA) Fluoroquinolone + Rifampin combination
3. Undulant fever/ Brucellosis	Doxycycline + Rifampin TMP-SMZ + Gentamicin Ciprofloxacin + Rifampin
4. *Clostridium sp*	Penicillin Metronidazole Clindamycin Imipenem Meropenem Vancomycin (4)
5. Haemophilus influenzae	Respiratory infections: • Ampicillin + Clavulanate • Doxycycline • Azithromycin • Ceftriaxone • Cefuroxime • TMP-SMZ Meningitis and other serious infections: • Ceftriaxone
6. Legionella (Pontiac fever)	Azithromycin, or fluoroquinolones $\overline{+}$ rifampin Doxycycline $\overline{+}$ rifampin
7. Mycobacterium Fever 7a-*M.avium* complex 7b-*M.fortuitum-chelonei* 7c-*M.kansaii* 7d-*M.leprae* 7e-*M.tuberculosis*	7a-Clarithromycin or azithromycin + Ethambutol, $\overline{+}$ rifabutin. Amikacin, ciprofloxacin 7b-Cefoxitin + clarithromycin Amikacin, rifampin, sulfonamide, doxycycline, linezolid 7c-INH + rifampin $\overline{+}$ ethambutol Clarithromycin, azithromycin, ethionamide, cycloserine 7d-Dapsone + rifampin $\overline{+}$ clofazimine Minocycline, ofloxacin, clarithromycin 7e-INH + rifampin + pyrazinamide $\overline{+}$ ethambutol Rifapentine, Streptomycin (increasing resistance)
8. Typhoid fever Salmonella sp.	Ceftriaxone Fluoroquinolones: Ciprofloxacin, Levofloxacin, Moxifloxacin
9. Relapsing fever *Borrelia recurrentis*	Doxycycline Penicillin Tetracycline Erythromycin
10. Coagulase negative Staphylococcus: *S.saprophyticus* *S.epidermidis* *S.haemolyticus* *S.hominis* *S. warneri* *S.saccharolyticus*	Vancomycin Vancomycin and Rifampin combination therapy with Gentamicin for MRS strains

11. *Streptococcus pneumoniae* associated fevers	Amoxicillin for penicillin susceptible strains (2) Azithromycin or Clarithromycin if allergic to penicillin Doxycycline Levofloxacin Gemifloxacin Moxifloxacin Penicillin G Ceftriaxone Vancomycin for penicillin highly resistant strains
12. Bartonella Fever 12a B.henselae 12b B.quintana	12a-b • Doxycycline + Gentamicin • Doxycycline + Rifampin
13. Escherichia coli 13a- Shiga toxin producing/ STEC 13b-ECET enterotoxigenic	13a- Self-limited 5-10 days. Associated to hemolytic uremic (HUS) syndrome in children. Antibiotics are avoided because the increased risk of HUS. 13b- Fluoroquinolones: Ciprofloxacin, Levofloxacin, Moxifloxacin
14. *Shiguella sp.* Induced fever	Fluoroquinolones: Ciprofloxacin, Levofloxacin, Moxifloxacin Azithromycin Ampicillin TMP-SMZ Ceftriaxone
15. *Yerssinia enterocolitica*	Tetracyclines Fluoroquinolones
16. *Moraxella catarrhalis*	Cefuroxime Fluoroquinolones: Ciprofloxacin, Levofloxacin, Moxifloxacin Ceftriaxone Cefuroxime axetil Erythromycin Minocycline Azithromycin Amoxicillin-Clavulanic TMP-SMZ
17. *Mycoplasma pneumoniae*	Clarithromycin Azithromycin Doxycycline Fluoroquinolones: Ciprofloxacin, Levofloxacin, Moxifloxacin Erythromycin
18. *Neisseria meningitidis*	Penicillin if sensitive Ceftriaxone Ampicillin REFERENCES—42,43,44, and 45

Prevention, and control of bacterial fevers:

Scarlet fever:

Scarlet fever is a syndrome characterized by exudative pharyngitis, fever, and bright-red exanthem.

Scarlet fever may follow streptococcal wound infections or burns, as well as upper respiratory tract infections.

The causative agent in scarlet fever is GAS, a gram-positive coccus that grows in chains. Scarlet fever is caused by the release of pyogenic exotoxins A,B,C

In cases associated with pharyngitis, lack of a cough, exudates, cervical nodes, temperature, and age (less than 15 years) help determine the likelihood of strep throat.

The bacteria is the causative agent of strep throat, impetigo, erysipelas, cellulitis, and necrotizing fasciitis.

Spread:

The spread of infection is promoted by mucosal transfer of bacteria to others via an environment of close proximity found in classrooms and similar workplace settings. _ _ _There are no specific histological changes in scarlet fever. One will observe neutrophilic infiltrate with spongiosis and parakeratosis in the epidermis.

Rheumatic fever *Streptococcus pyogenes:*

The development of ARF occurs approximately two weeks after *S. pyogenes* infection Acute rheumatic fever is a delayed sequel of pharyngitis due to Streptococcus pyogenes, which are also called group A Streptococcus or group A strep. The exact disease process is not fully known. However, the disease is in part due to an autoimmune response to *S. pyogenes* infection involving multiple organ systems. Organ systems involved typically include the heart, joints, and central nervous system. Autoimmune cross-reaction of anti-streptococcal antibodies with antigen of joints and heart tissues.

Streptococcal pharyngitis typically precedes the onset of acute rheumatic fever by 1 to 5 weeks.*S. pyogenes* are gram-positive cocci that grow in chains. They exhibit ß-hemolysis. The differential diagnosis may include but is not limited to: rheumatoid arthritis, juvenile idiopathic arthritis, septic arthritis, systemic lupus erythematosus, serum sickness, Lyme disease, infective endocarditis, viral myocarditis, Henoch-Schonlein purpura, gout, sarcoidosis, leukemia, and Hodgkin's disease.1

Patients with acute rheumatic fever should start on therapy including salicylates and anti-inflammatory medicines to relieve inflammation and decrease fever, as well as management of cardiac failure. Rheumatic heart disease is the most

important long-term sequel of acute rheumatic fever due to its ability to cause disability or death.

Undulant fever/Brucellosis:
Brucella melitensis is the most aggressive strain which produces malignant type of human disease. It is zoonotic Infection does not appear to spread from man to man. Clinical findings are malaise, fever, weakness, aches and sweats. The fever usually rises in the afternoon. Its fall during the night is accompanied by drenching sweat.

Prevention and control:
Brucellosis can be transmitted by contact with infected tissues, blood, urine, vaginal discharges, aborted animal fetuses and especially placentae. It can also be transmitted by the ingestion of raw milk and milk products from infected animals.

Outbreaks are generally attributed to the inhalation of aerosols, or through the ingestion of unpasteurized milk products.

Bartonella Fever:
In 1909, Dr. Alberto Barton discovered the organism that became named Bartonella bacilliforms. It causes Oroya fever. It is transmitted through sand flies.

Oroya fever is characterized by rapid development of severe anemia due to blood destruction, enlargement of spleen, liver and hemorrhage into the lymph nodes.

Human diseases caused by the Bartonella spp bacteria include cat scratch disease *(Bartonella henselae), Carrion's disease (Bartonella bacilliforms),* and *trench fever (Bartonella Quintana).*

Control:
Elimination of sand flies. Insecticides, insect repellents can be used. Prevention with antibiotics may be useful.

Legionella (Pontiac fever):
The Pontiac fever illness shows high fever, chills, malaise, nonproductive cough, hypoxia, diarrhea, and delirium

Symptoms begin between a few hours to 3 days after being exposed to the bacteria and usually last less than a week. Pontiac fever is different from Legionnaires' disease because someone with Pontiac fever does not have pneumonia.

Pontiac fever is a mild flu-like illness caused by exposure to Legionella bacteria, which is found in water.

Persons of any age are at risk for Pontiac fever. Pontiac fever is spread by breathing in water droplets in the air that contain Legionella bacteria.

Control:
Chlorination and heating up of water and cleaning can help control the multiplication of *Legionellae* in water and air conditioning systems

Relapsing fever (Borrelia):
Relapsing fever is endemic in many parts of the world. It is main reservoir of rodent population Relapsing fever is a recurring febrile disease caused by several species of the spirochete Borrelia and transmitted by lice or ticks. Pathogenic spirochetes include Treponema, Leptospira, and Borrelia. Symptoms are headache, myalgia, and vomiting There are three types of relapsing fever: Tick-borne relapsing fever (TBRF) Louse-borne relapsing fever (LBRF) Borrelia miyamotoi disease (sometimes called hard tick relapsing fever) TBRF occurs in the western United States and is usually linked to sleeping in rustic, rodent-infested cabins in the mountains.

Prevention and control:
Prevention is based on avoidance of exposure to ticks and lice and on delousing (cleanliness and insecticide) No vaccines are available.

Q-Fever-Coxiella:
Q fever is a disease caused by the bacteria *Coxiella burnetii.* This bacteria naturally infects some animals, such as goats, sheep, and cattle. *C. burnetii* bacteria are found in the birth products (i.e. placenta, amniotic fluid), urine, feces, and milk of infected animals. *C. burnetii* has been previously weaponized for use in biological warfare and is considered a potential terrorist threat. _ *C. burnetii* is a highly infectious agent, in some cases requiring less than 10 bacteria to make you sick. C.

CONCLUSION:
Many bacteria are causing fevers. Fever, at a molecular level, affects cells. Cellular membranes are key elements in the entry of several pathogens. In that process key aspects such as lipid composition or fluidity can be directly affected by pyrexia. Enzymatic reactions are also dependent on temperature, and there is a potential impact of fever on normal metabolic flux. Pyrexia does not necessarily need to be treated, Damage to the brain generally does not occur until temperatures reach 42 °C (107.6 °F), and it is rare for an untreated fever to exceed 40.6 °C (105 °F).Sponging or bathing feverish children with moderately warm water. Fan or air conditioning may somewhat reduce the temperature and increase comfort. In Hyperpyrexia patients, aggressive cooling is required (generally produced mechanically via conduction by applying numerous ice packs across most of the body or direct submersion in ice water). Use of *antipyretics reduces fever.*

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